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This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (currently amended) A compound of formula

$$Q \xrightarrow{N} a^{1} a^{2} a^{3} \qquad (I)$$

a an ester or amide prodrug, N-oxide, addition salt, quaternary amine, metal complex or stereochemically isomeric form thereof

wherein $-a^1=a^2-a^3=a^4$ represents a bivalent radical of formula

$$-CH=CH-CH=CH- (a-1);$$

wherein each hydrogen atom in the radical (a-1) may optionally be replaced by halo, C_{1-6} alkyl, nitro, amino, hydroxy, C_{1-6} alkyloxy, polyhalo C_{1-6} alkyl, carboxyl, amino C_{1-6} alkyl, mono- or di(C_{1-4} alkyl)amino C_{1-6} alkyl, C_{1-6} alkyloxycarbonyl, hydroxy C_{1-6} alkyl, or a radical of formula

wherein =Z is =O, =CH-C(=O)-NR 5a R 5b , =CH $_2$, =CH-C $_{1-6}$ alkyl, =N-OH or =N-O-C $_{1-6}$ alkyl;

Q is a radical of formula

$$R^{2}$$
 R^{4}
 R^{2}
 R^{2}
 R^{4}
 R^{2}
 R^{2

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wherein

Alk is C₁₋₆alkanediyl;

Y¹ is a bivalent radical of formula –NR²- or –CH(NR²R⁴)-;

X¹ is NR⁴, S, S(=O), S(=O)₂, O, CH₂, C(=O), C(=CH₂), CH(OH), CH(CH₃), CH(OCH₃), CH(SCH₃), CH(NR^{5a}R^{5b}), CH₂-NR⁴ or NR⁴-CH₂;

X² is a direct bond, CH₂, C(=0), NR⁴, C₁₋₄alkylene-NR⁴, or NR⁴-C₁₋₄alkylene C₁₋₄alkyl-NR⁴, NR⁴-C₁₋₄alkyl;

t is 2, 3, 4 or 5;

u is 1, 2, 3, 4 or 5;

v is 2 or 3; and

whereby each hydrogen atom in Alk and the carbocycles and the heterocycles defined in radicals (b-3), (b-4), (b-5), (b-6), (b-7) and (b-8) may optionally be replaced by R^3 ; with the proviso that when R^3 is hydroxy or C_{1-6} alkyloxy, then R^3 can not replace a hydrogen atom in the α position relative to a nitrogen atom;

G is a direct bond or C_{1-10} alkanediyl optionally substituted with one, two or three substituents selected from hydroxy, C_{1-6} alkyloxy, aryl C_{1-6} alkylthio, aryl C_{1-6} alkylthio, arylcarbonyl, HO(-CH₂-CH₂-O)_n-, C_{1-6} alkyloxy(-CH₂-CH₂-O)_n-, aryl C_{1-6} alkyloxy(-CH₂-CH₂-O)_n-, amino, mono-or di(C_{1-6} alkyl)amino, C_{1-6} alkyloxycarbonylamino and aryl;

R¹ is a bicyclic heterocycle selected from quinolinyl, <u>isoquinolinyl</u>, quinoxalinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, pyridopyridyl, naphthiridinyl, 1*H*-imidazo[4,5-b]pyridinyl, 3*H*-imidazo[4,5-b]pyridinyl, imidazo[1,2-a]pyridinyl, 2,3-dihydro-1,4-dioxino[2,3-b]pyridyl or a radical of formula

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$$(CH_{2})_{m} \qquad (CH_{2})_{m} \qquad (CH_$$

and said bicyclic heterocycles may optionally be substituted in either of the two cycles with 1 or where possible more, such as 2, 3 or 4, substituents selected from halo, hydroxy, amino, cyano, carboxy, C₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkylthio, C₁₋₆alkyloxyC₁₋₆alkyl, arylC₁₋₆alkyl, arylC₁₋₆alkyloxy, hydroxyC₁₋₆alkyl, monoor di(C₁₋₆alkyl)amino, mono-or di(C₁₋₆alkyl)aminoC₁₋₆alkyl, polyhaloC₁₋₆alkyl, C₁₋₆alkylcarbonylamino, C₁₋₆alkyl-SO₂-NR^{5c}-, aryl-SO₂-NR^{5c}-, C₁₋₆alkyloxycarbonyl, -C(=O)-NR^{5c}R^{5d}, HO(-CH₂-CH₂-O)_n-, halo(-CH₂-CH₂-O)_n-, C₁₋₆alkyloxy(-CH₂-CH₂-O)_n-, arylC₁₋₆alkyloxy(-CH₂-CH₂-O)_n- and mono-or di(C₁₋₆alkyl)amino(-CH₂-CH₂-O)_n-;

each n independently is 1, 2, 3 or 4;

each m independently is 1 or 2;

each p independently is 1 or 2;

each R^2 independently is hydrogen, formyl, C_{1-6} alkylcarbonyl, Hetcarbonyl, pyrrolidinyl, piperidinyl, homopiperidinyl, C_{3-7} cycloalkyl substituted with $N(R^6)_2$, or C_{1-10} alkyl substituted with $N(R^6)_2$ and optionally with a second, third or fourth substituent selected from amino, hydroxy, C_{3-7} cycloalkyl, C_{2-5} alkanediyl, piperidinyl, mono-or di $(C_{1-6}$ alkyl)amino, C_{1-6} alkyloxycarbonylamino, aryl and aryloxy;

 R^3 is hydrogen, hydroxy, C_{1-6} alkyl, C_{1-6} alkyloxy, aryl C_{1-6} alkyloxy;

R⁴ is hydrogen, C₁₋₆alkyl or arylC₁₋₆alkyl;

R^{5a}, R^{5b}, R^{5c} and R^{5d} each independently are hydrogen or C₁₋₆alkyl; or

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R^{5a} and R^{5b}, or R^{5c} and R^{5d} taken together form a bivalent radical of formula -(CH₂)_s- wherein s is 4 or 5;

 R^6 is hydrogen, C_{1-4} alkyl, formyl, hydroxy C_{1-6} alkyl, C_{1-6} alkylcarbonyl or C_{1-6} alkyloxycarbonyl;

aryl is phenyl or phenyl substituted with 1 or more, such as 2, 3 or 4, substituents selected from halo, hydroxy, C_{1-6} alkyl, hydroxy C_{1-6} alkyl, polyhalo C_{1-6} alkyl, and C_{1-6} alkyloxy; and

Het is pyridyl, pyrimidinyl, pyrazinyl, or pyridazinyl.

2. (cancelled)

- 3. (previously presented) A compound according to claim 1, wherein Q is a radical of formula (b-5) wherein v is 2 and Y^1 is -NR²-.
- 4. (previously presented) A compound according to claim 1, wherein R^2 is C_{1-10} alkyl substituted with NHR⁶.
- 5. (previously presented) A compound according to claim 1, wherein G is a direct bond or C₁₋₁₀alkanediyl optionally substituted with one, two or three substituents selected from hydroxy, C₁₋₆alkyloxy, arylC₁₋₆alkyloxy, HO(-CH₂-CH₂-O)_n-, C₁₋₆alkyloxy(-CH₂-CH₂-O)_n-, arylC₁₋₆alkyloxy(-CH₂-CH₂-O)_n-.
- 6. (currently amended) A compound according to claim 1, wherein the compound is (±)-N-[1-(2-aminoethyl)-4-piperidinyl]-4-methyl-1-[1-(8-quinolinyl)ethyl]-1H-benzimidazol-2-amine monohydrate;
 - (\pm) -N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(2-bromo-5,6,7,8-tetrahydro-8-quinolinyl)-IH-benzimidazol-2-amine trihydrochloride trihydrate;
 - (\pm) -N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-4-methyl-IH-benzimidazol-2-amine;
 - (\pm)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(2-chloro-5,6,7,8-tetrahydro-5-quinoxalinyl)-1H-benzimidazol-2-amine trihydrochloride trihydrate; Page 5 of 20

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- (\pm)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(1-methyl-1H-benzimidazol-4-yl)methyl]-1H-benzimidazol-2-amine;
- (\pm)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(ethoxy-8-quinolinylmethyl)-IH-benzimidazol-2-amine;
- (\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-4-methyl-1-(5,6,7,8-tetrahydro-5-quinoxalinyl)-*1H*-benzimidazol-2-amine;
- N-[1-(2-aminoethyl)-4-piperidinyl]-4-methyl-1-(8-quinolinylmethyl)-1H-benzimidazol-2-amine;
- N-[1-(8-quinolinylmethyl)-1H-benzimidazol-2-yl]-1,3-propanediamine trihydrochloride monohydrate;
- (\pm)-N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-1H-benzimidazol-2-amine trihydrochloride dihydrate;
- (\pm)-N-[1-[1-(aminomethyl)-2-methylpropyl]-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-1H-benzimidazol-2-amine;
- (\pm)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(1-isoquinolinylmethyl)-1H-benzimidazol-2-amine trihydrochloride trihydrate;
- *N*-[1-(2-aminoethyl)-4-piperidinyl]-1-(5,6,7,8-tetrahydro-5-quinoxalinyl)-*1H*-benzimidazol-2-amine trihydrochloride trihydrate;
- (\pm)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-4-methyl-1-(8-quinolinylmethyl)-1H-benzimidazol-2-amine;
- (±)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-1-(2-chloro-5,6,7,8-tetrahydro-5-quinoxalinyl)-4-methyl-*1H*-benzimidazol-2-amine trihydrochloride trihydrate;
- (\pm)-*N*-[1-(2-aminoethyl)-4-piperidinyl]-1-(5,6,7,8-tetrahydro-2,3-dimethyl-5-quinoxalinyl)-*1H*-benzimidazol-2-amine trihydrochloride trihydrate;
- (\pm)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-1H-benzimidazol-2-amine;
- (±)-N-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(3-chloro-5,6,7,8-tetrahydro-5-quinoxalinyl)-1H-benzimidazol-2-amine trihydrochloride monohydrate;
- (±)-N-[1-(2-aminoethyl)-4-piperidinyl]-1-(3-chloro-5,6,7,8-tetrahydro-5-quinoxalinyl)-4-methyl-1H-benzimidazol-2-amine trihydrochloride dihydrate;

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(\pm)-N-[1-(2-aminoethyl)-4-piperidinyl]-1-[(2-ethoxyethoxy)-8-quinolinylmethyl]-4-methyl-IH-benzimidazol-2-amine monohydrate;

(\pm)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-4-methyl-1-[(1-methyl-1H-benzimidazol-4-yl)methyl]-1H-benzimidazol-2-amine;

(±)-*N*-[1-(2-amino-3-methylbutyl)-4-piperidinyl]-1-(2-chloro-5,6,7,8-tetrahydro-5-quinoxalinyl)-4-methyl-*1H*-benzimidazol-2-amine;

- **a** an ester or amide prodrug, N-oxide, addition salt, quaternary amine, metal complex or stereochemically isomeric form thereof.
- 7. (previously presented) A method of treating a respiratory syncytial viral infection, comprising the step of administering a therapeutically effective amount of a compound as claimed in any one of claims 1 and 3 to 6.
- 8. (previously presented) A pharmaceutical composition, comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as claimed in any one of claims 1 and 3 to 6.
- 9. (previously presented) A process of preparing a composition as claimed in claim 8, comprising the step of intimately mixing said carrier with said compound.
- 10. (original) An intermediate of formula

$$P \longrightarrow Q_1 \longrightarrow N \longrightarrow \begin{bmatrix} a^1 \\ a^2 \\ a^4 \end{bmatrix} = a^2$$
 (IV)

with R^1 , G and $-a^1=a^2-a^3=a^4$ defined as in claim 1, P being a protective group, and Q_1 being defined as Q according to claim 1 but being devoided of the R^2 or R^6 substituent.

11. (original) An intermediate of formula

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$$(O =)Q_3 - (IX)$$

with R^1 , G and $-a^1=a^2-a^3=a^4$ defined as in claim 1, and $(O=)Q_3$ being a carbonyl derivative of Q, said Q being defined according to claim 1, provided that it is devoided of the NR^2R^4 or NR^2 substituent.

12. (original) An intermediate of formula

$$Q \xrightarrow{N} A^{1} A^{2} A^{3}$$
(XXII)

with R^1 , Q and $-a^1=a^2-a^3=a^4$ defined as in claim 1, and $(O=)G_2$ being a carbonyl derivative of G, said G being defined according to claim 1.

- 13. (currently amended) A process of preparing a compound as claimed in claim 1, comprising at least one step selected from the group consisting of:
 - a) reacting an intermediate of formula (II-a) or (II-b) with an intermediate of formula (III)

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$$R^{1}$$
 R^{1}
 R^{1

with R^1 , G, Q and $-a^1=a^2-a^3=a^4$ - defined as in claim 1, and W_1 being a suitable leaving group, in the presence of a suitable base and in a suitable reaction-inert solvent;

b) deprotecting an intermediate of formula (IV)

$$P = Q_1 = \begin{bmatrix} R^1 \\ N \\ A^4 = A^3 \end{bmatrix}$$

$$H = Q_1 = \begin{bmatrix} R^1 \\ N \\ A^4 = A^3 \end{bmatrix}$$

$$(IV)$$

$$(I-a)$$

with R^1 , G, and $-a^1=a^2-a^3=a^4$ defined as in claim 1, H-Q₁ being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is hydrogen, and P being a protective group;

c) deprotecting and reducing an intermediate of formula (IV-a)

$$P \longrightarrow Q_{1a}(CH=CH) \longrightarrow N \longrightarrow a^{1 \atop a^{2} \atop a^{3}} \longrightarrow H \longrightarrow Q_{1} \longrightarrow N \longrightarrow a^{1 \atop a^{2} \atop a^{3}}$$

$$(IV-a) \qquad (I-a)$$

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with R^1 , G, and $-a^1=a^2-a^3=a^4$ defined as in claim 1, H-Q₁ being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is hydrogen, Q_{1a}(CH=CH) being defined as Q₁ provided that Q₁ comprises an unsaturated bond, and P being a protective group;

d) deprotecting an intermediate of formula (V)

with R^1 , G, and $-a^1=a^2-a^3=a^4$ - defined as in claim 1, and H_2N-Q_2 being defined as Q according to claim 1 provided that both R^6 substituents are hydrogen or R^2 and R^4 are both hydrogen;

e) deprotecting an intermediate of formula (VI)

$$P = P = Q_{2} = N$$

$$= N - Q_{$$

with R^1 , G, and $-a^1=a^2-a^3=a^4$ - defined as in claim 1, and H_2N-Q_2 being defined as Q according to claim 1 provided that both R^6 substituents are hydrogen or R^2 and R^4 are both hydrogen, and P being a protective group;

f) deprotecting an intermediate of formula (VII) or (VIII)

$$P = Q_{1'}(OP) = \begin{pmatrix} R^1 & & & \\ & & &$$

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$$P = N - Q_{2'}(OP) - N - Q_{2'}(OH) - N - Q_{2'}(OH) - N - Q_{2'}(OH) - N - Q_{2'}(OH) - Q_{2'$$

with R^1 , G, and $-a^1=a^2-a^3=a^4$ defined as in claim 1, H-Q₁·(OH) being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is hydrogen and provided that Q comprises a hydroxy moiety, H₂N-Q₂·(OH) being defined as Q according to claim 1 provided that both R^6 substituents are hydrogen or R^2 and R^4 are both hydrogen and provided that Q comprises a hydroxy moiety, and P being a protective group;

g) amination of an intermediate of formula (IX)

with R^1 , G, and $-a^1=a^2-a^3=a^4$ - defined as in claim 1, and H_2N-Q_3H being defined as Q according to claim 1 provided that both R^6 substituents are hydrogen or R^2 and R^4 are both hydrogen, and the carbon adjacent to the nitrogen carrying the R^6 , or R^2 and R^4 substituents contains at least one hydrogen, in the presence of a suitable amination reagent;

h) reducing an intermediate of formula (X)

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with R^1 , G, and $-a^1=a^2-a^3=a^4$ - defined as in claim 1, and $H_2N-CH_2-Q_4$ being defined as Q according to claim 1 provided that Q comprises a $-CH_2-NH_2$ moiety, in the presence of a suitable reducing agent;

i) reducing an intermediate of formula (X-a)

with G, and $-a^1=a^2-a^3=a^4$ defined as in claim 1, $H_2N-CH_2-Q_4$ being defined as Q according to claim 1 provided that Q comprises a $-CH_2-NH_2$ moiety, and R^1 being defined as R^1 according to claim 1 provided that it comprises at least one substituent, in the presence of a suitable reducing agent and suitable solvent;

j) amination of an intermediate of formula (XI)

with R¹, G, and -a¹=a²-a³=a⁴- defined as in claim 1, and H₂N-CH₂-CHOH-

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CH₂-Q₄· being defined as Q according to claim 1 provided that Q comprises a CH₂-CHOH-CH₂-NH₂ moiety, in the presence of a suitable amination reagent;

k) reacting an intermediate of formula (XII) with formic acid, formamide and ammonia

$$C_{1-4}alkyl - C_{1-4}C_{1-4$$

with R^1 , G, and $-a^1=a^2-a^3=a^4$ defined as in claim 1, and H-C(=O)- Q_1 being defined as Q according to claim 1 provided that R^2 or at least one R^6 substituent is formyl;

1) amination of an intermediate of formula (XIII) by reaction with an intermediate of formula (XIV)

$$(O=)Q_{5} \xrightarrow{R^{1}} A^{2} A^{2} A^{3} + R^{2a} - NH_{2}$$
 amination
$$R^{2a} - NH - HQ_{5}$$
 (XIII)
$$(XIV)$$
 (I-c)

with R¹, G, and -a¹=a²-a³=a⁴- defined as in claim 1, and R^{2a}-NH-HQ₅ being defined as Q according to claim 1 provided that R² is other than hydrogen and is represented by R^{2a}, R⁴ is hydrogen, and the carbon atom adjacent to the nitrogen atom carrying the R² and R⁴ substituents, carries also at least one hydrogen atom, in the presence of a suitable reducing agent;

m) reducing an intermediate of formula (XV)

$$(R^{6})_{2}N-(C_{1}-\text{palkyl})-NH-HQ_{5}$$

$$C(=O)OC_{1}-\text{palkyl}$$

$$(XV)$$

$$R^{1}$$

$$a^{1}$$

$$a^{2}$$

$$A^{2}$$

$$A^{3}$$

$$A^{2}$$

$$A^{3}$$

$$A^{4}$$

$$A^{3}$$

$$A^{4}$$

$$A^{3}$$

$$A^{4}$$

$$A^{3}$$

$$A^{4}$$

$$A^{3}$$

$$A^{4}$$

$$A^{3}$$

$$A^{4}$$

$$A^$$

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with R^1 , G, and $-a^1=a^2-a^3=a^4$ - defined as in claim 1, and $(R^6)_2N$ -[$(C_{1.9}alkyl)CH_2OH$]-NH-HQ5 being defined as Q according to claim 1 provided that R^2 is other than hydrogen and is represented by $C_{1.10}alkyl$ substituted with $N(R_6)_2$ and with hydroxy, and the carbon atom carrying the hydroxy, carries also two hydrogen atoms, and provided that R^4 is hydrogen, and the carbon atom adjacent to the nitrogen atom carrying the R^2 and R^4 substituents, carries also at least one hydrogen atom, with a suitable reducing agent;

n) deprotecting an intermediate of formula (XVI), (XVI-a) or (XVI-b)

$$(A - O - P)_{w}$$

$$R^{1a}$$

$$(A - O - H)_{w}$$

$$R^{1a}$$

$$A - O - H$$

$$A - A - O - H$$

$$A - A - O - H$$

$$A - O - H$$

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with G, and $-a^1=a^2-a^3=a^4$ defined as in claim 1, and H-Q₁ being defined as Q according to claim 1 provided that R² or at least one R⁶ substituent is hydrogen, and R^{1a}-(A-O-H)_w, R^{1a'}-(A-O-H)₂ and R^{1a''}-(A-O-H)₃ being defined as R¹ according to claim 1 provided that R¹ is substituted with hydroxy, hydroxyC₁₋₆alkyl, or HO(-CH₂-CH₂-O)_n-, with w being an integer from 1 to 4 and P or P₁ being a suitable protecting group, with a suitable acid- $\frac{1}{2}$

o) amination of an intermediate of formula (XVII)

$$C_{1^{-4}alkyl} \longrightarrow C_{-Alk} \longrightarrow R^{2}R^{4}N \longrightarrow$$

with R^1 , G, $-a^1=a^2-a^3=a^4$ -, Alk, X^1 R^2 and R^4 defined as in claim 1, in the presence of a suitable amination agent;

p) amination of an intermediate of formula (XIX)

$$H = C - C_{1-3} \text{alkyl} - NR^4$$

$$N = A^4 - A^3 + Q_6 N - CH_2 - C_{1-3} \text{alkyl} - NR^4 - A^3 - A^$$

with R^1 , G, and $-a^1=a^2-a^3=a^4$ - defined as in claim 1, and $Q_6N-CH_2-C_{1-3}$ alkyl- NR^4 being defined as Q according to claim 1 provided that in the definition of Q, X^2 is C_{2-4} alkyl- NR^4 , in the presence of a suitable amination agent;

q) deprotecting an intermediate of formula (XXI)

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with R^1 , Q, and $-a^1=a^2-a^3=a^4$ - defined as in claim 1, and HO-G₁ being defined as G according to claim 1 provided that G is substituted with hydroxy or HO-(CH₂CH₂O-)_n; and

r) reducing an intermediate of formula (XXII)

$$Q = \bigvee_{N = a^{1} = a^{2} = a^{2}}^{R^{1}}$$
reduction
$$Q = \bigvee_{N = a^{1} = a^{2} = a^{2} = a^{2}}^{R^{1}}$$

$$Q = \bigvee_{N = a^{1} = a^{2} = a^{2}$$

with R^1 , Q, and $-a^1=a^2-a^3=a^4$ - defined as in claim 1, and H-G₂-OH being defined as G according to claim 1 provided that G is substituted with hydroxy and the carbon atom carrying the hydroxy substituent carries also at least one hydrogen, in the presence of a suitable reducing agent.

14. (cancelled)

15. (cancelled)

- 16. (previously added) The process of claim 13, further comprising the step of converting compound of formula (I'), stereochemically isomeric forms, metal complexes, quaternary amines or N-oxide forms thereof, into a therapeutically active non-toxic acid addition salt by treatment with an acid.
- 17. (previously added) The process of claim 13, further comprising the step of converting compound of formula (I'), stereochemically isomeric forms, metal complexes, quaternary amines or N-oxide forms thereof, into a therapeutically active non-toxic base addition salt by treatment with alkali.
- 18. (previously added) The process of claim 13, further comprising the step of converting the acid addition salt form of compound of formula (I'), stereochemically Page 16 of 20

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isomeric forms, metal complexes, quaternary amines or N-oxide forms thereof, into the free base by treatment with alkali.

19. (previously added) The process of claim 13, further comprising the step of converting the base addition salt form of compound of formula (I'), stereochemically isomeric forms, metal complexes, quaternary amines or N-oxide forms thereof, into the free acid by treatment with acid.